

PCT

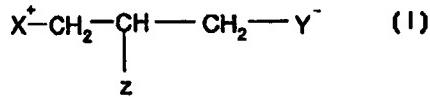
WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07C 229/22, 271/22, 275/16, C07D 257/04, C07F 9/54, 9/6561, A61K 31/195, 31/41, 31/66		A1	(11) International Publication Number: WO 99/59957 (43) International Publication Date: 25 November 1999 (25.11.99)
(21) International Application Number:	PCT/IT99/00126		
(22) International Filing Date:	11 May 1999 (11.05.99)		
(30) Priority Data:	MI98A001075 15 May 1998 (15.05.98)	IT	
(71) Applicant (for all designated States except US): SIGMA-TAU INDUSTRIE FARMACEUTICHE RIUNITE S.P.A. [IT/IT]; Viale Shakespeare, 47, I-00144 Rome (IT).			(74) Agent: SPADARO, Marco; Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Viale Shakespeare, 47, I-00144 Rome (IT).
(72) Inventors; and			
(75) Inventors/Applicants (for US only): GIANNESI, Fabio [IT/IT]; Via Berlinguer, 7, I-00040 Pomezia (IT). MARZI, Mauro [IT/IT]; Via Antonio Ciamparra, 158, I-00169 Rome (IT). MINETTI, Patrizia [IT/IT]; Via Nanchino, 28, I-00144 Rome (IT). DE ANGELIS, Francesco [IT/IT]; Piazza A. Frigeri, 13, I-00136 Rome (IT). TINTI, Maria, Ornella [IT/IT]; Via Ernesto Basile, 81, I-00182 Rome (IT). CHIODI, Piero [IT/IT]; Via Trento, 3, I-00043 Ciampino (IT). ARDUINI, Arduino [IT/IT]; Via della Camilluccia, 701, I-00135 Rome (IT).			(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
			Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: COMPOUNDS HAVING REVERSIBLE INHIBITING ACTIVITY OF CARNITINE PALMITOYL-TRANSFERASE



(57) Abstract

Compounds of formula (I) wherein the groups are as defined in the description are disclosed. The compounds of formula (I) are endowed with reversible inhibiting activity of carnitine palmitoyl-transferase and are useful in the preparation of medicaments useful in the pathologies related to a hyperactivity of carnitine palmitoyl-transferase, such as hyperglycemia, diabetes and pathologies related thereto, heart failure, ischemia.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IT 99/00126

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 6	C07C229/22	C07C271/22	C07C275/16	C07D257/04	C07F9/54
	C07F9/6561	A61K31/195	A61K31/41	A61K31/66	

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07C C07D C07F A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 25197 A (AFFYMAX TECHNOLOGIES) 23 December 1993 (1993-12-23) page 135, line 35 - page 136, line 21 -----	1,2
X	ZHI-HENG HUANG ET AL.: "Analysis of Acylcarnitines as Their N-Demethylated Ester Derivatives by Gas Chromatography-Chemical Ionization Mass Spectrometry" ANALYTICAL BIOCHEMISTRY., vol. 199, no. 1, 15 November 1991 (1991-11-15), pages 98-105, XP002115164 ACADEMIC PRESS INC. NEW YORK., US ISSN: 0003-2697 page 99, scheme 1; page 102, figure 7 ----- -/-	1,2

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

13 September 1999

Date of mailing of the international search report

28/09/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl
Fax: (+31-70) 340-3016

Authorized officer

Zervas, B

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IT 99/00126

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 00389 A (SANG JEW ET AL.) 8 January 1998 (1998-01-08) page 1 - page 2; claims ----	1, 13
A	US 5 196 418 A (RICHARD D. GANDOUR ET AL.) 23 March 1993 (1993-03-23) claims ----	1, 13
A	EP 0 574 355 A (SANDOZ) 15 December 1993 (1993-12-15) cited in the application claims -----	1, 13
A	WO 85 04396 A (CORNELL RESEARCH FOUNDATION) 10 October 1985 (1985-10-10) cited in the application claims -----	1, 13

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IT 99/00126

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: **19, 22, 26 and 27**

because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 19, 22, 26 and 27

are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.

2. Claims Nos.:

because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No	
PCT/IT/99/00126	

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9325197	A 23-12-1993	AU 4534593 A		04-01-1994
		EP 0647133 A		12-04-1995
		US 5814603 A		29-09-1998
		US 5622944 A		22-04-1997
		US 5607691 A		04-03-1997
		AU 6764794 A		29-08-1994
		CA 2153243 A		18-08-1994
		EP 0683668 A		29-11-1995
		JP 8510720 T		12-11-1996
		WO 9417792 A		18-08-1994
WO 9800389	A 08-01-1998	AU 3464497 A		21-01-1998
US 5196418	A 23-03-1993	NONE		
EP 574355	A 15-12-1993	AT 156828 T		15-08-1997
		AU 667537 B		28-03-1996
		CA 2098133 A		12-12-1993
		CN 1086217 A,B		04-05-1994
		CZ 9301083 A		15-02-1995
		DE 69313029 D		18-09-1997
		DE 69313029 T		29-01-1998
		DK 574355 T		26-01-1998
		ES 2105194 T		16-10-1997
		FI 932662 A		12-12-1993
		GR 3024684 T		31-12-1997
		HU 65327 A		02-05-1994
		HU 9500248 A		28-11-1995
		IL 105965 A		18-03-1997
		JP 6073077 A		15-03-1994
		NO 932096 A		13-12-1993
		NZ 247840 A		27-04-1995
		SG 42983 A		17-10-1997
		SK 58893 A		08-06-1994
		US 5516767 A		14-05-1996
		ZA 9304157 A		05-09-1994
WO 8504396	A 10-10-1985	AT 48832 T		15-01-1990
		AU 570112 B		03-03-1988
		AU 4216685 A		01-11-1985
		CA 1297901 A		24-03-1992
		EP 0177574 A		16-04-1986
		JP 6062523 B		17-08-1994
		JP 61501776 T		21-08-1986
		US 4781863 A		01-11-1988